Diagnosis and Treatment of Meningitis

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Practice Guidelines for the Management of Bacterial Meningitis (Archived)

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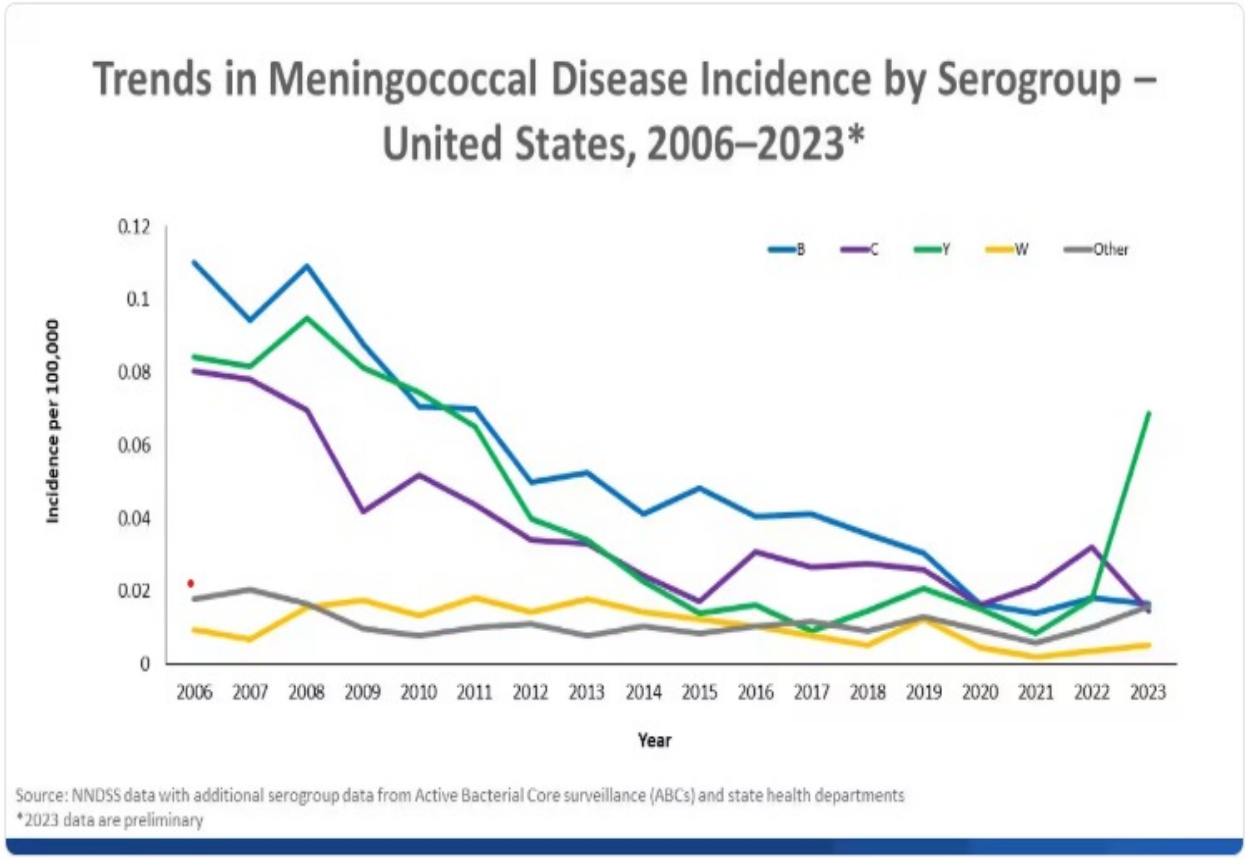
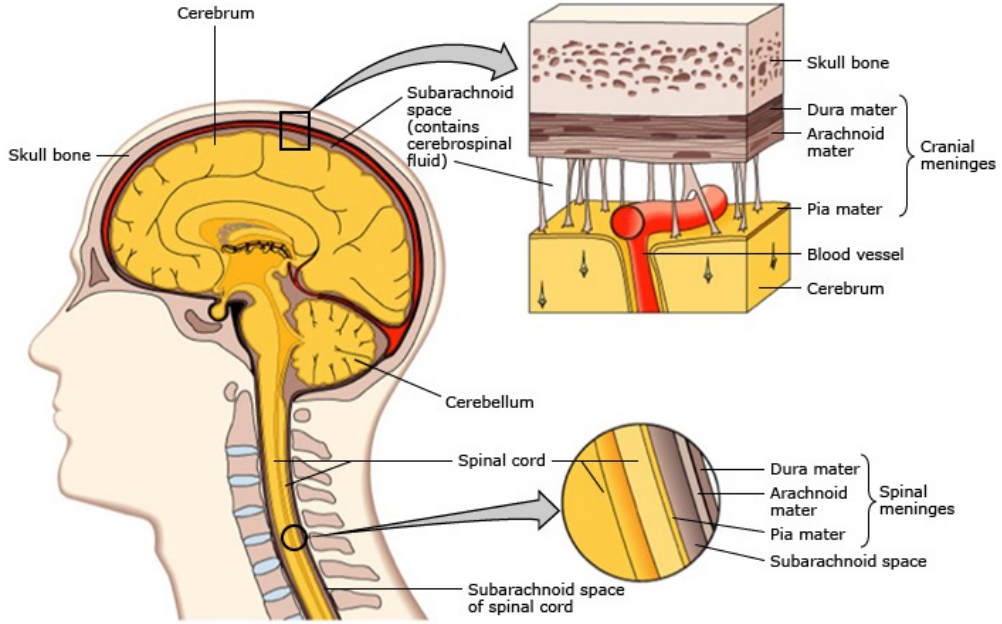
Meningitis Epidemiology

- Incidence of bacterial meningitis declined significantly in the US after introduction of the *H. influenzae* type b, meningococcal and pneumococcal vaccines
- Peak incidence now occurs in adults (vs. previously was in children < 5 years of age)



Meningitis Pathophysiology

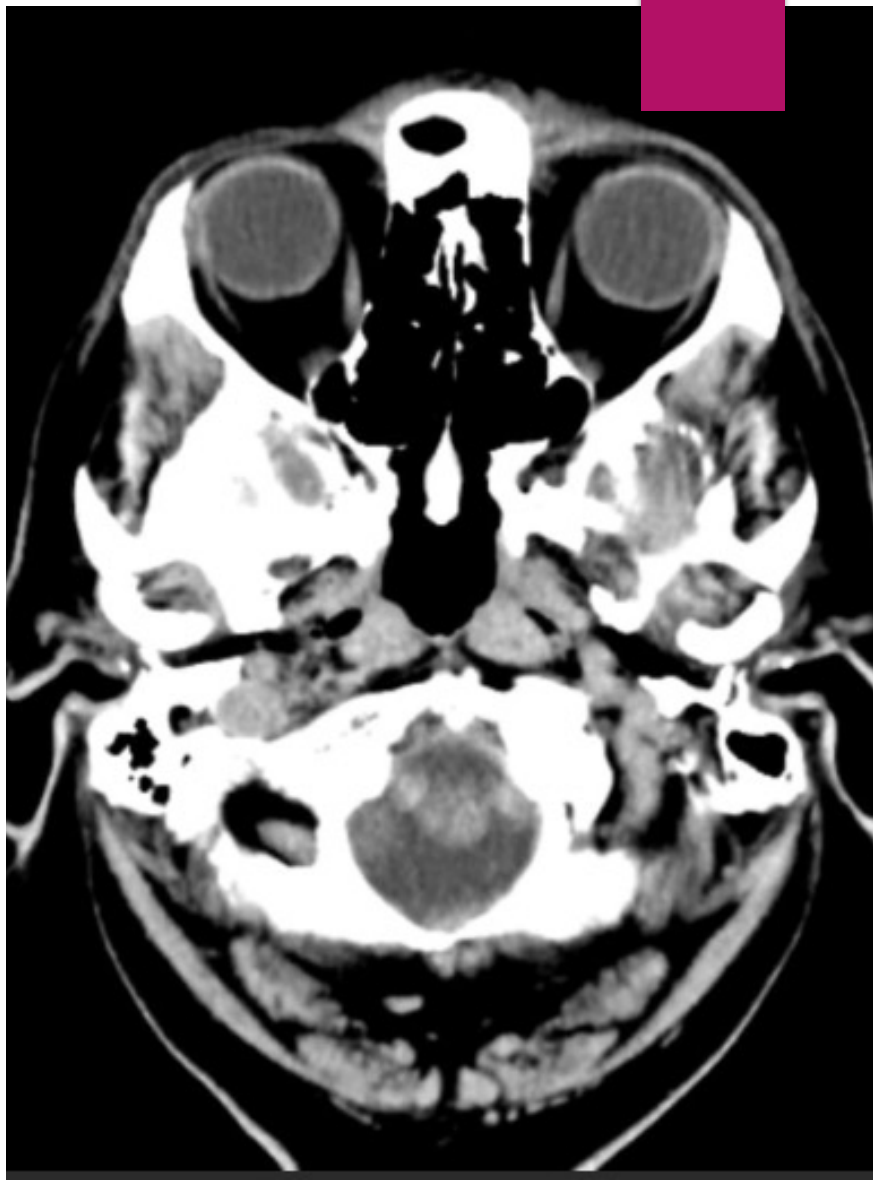
- Infection of the arachnoid mater and the CSF in both the subarachnoid space and the cerebral ventricles
- **Classic triad:** fever, nuchal rigidity and change in mental status (all 3 only occur in ~ 40% of patients)
- In a 2004 prospective study of 696 cases of community-acquired bacterial meningitis, almost all patients (95%) presented with at least two of four symptoms (headache, fever, stiff neck, and altered mental status)



Clinical features and prognostic factors in adults with bacterial meningitis. AU van de Beek D, de Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M SO N Engl J Med. 2004; 351(18):1849.

Meningitis: work-up

- Obtain blood cultures and CSF samples as soon as the diagnosis is suspected
- When to do a head CT prior to lumbar puncture?
  - History of CNS disease (mass lesion, stroke, focal infection)
  - New onset seizure (within 1 week)
  - Papilledema or focal neurologic deficit
  - Abnormal level of consciousness
  - Immunocompromised



	Glucose (mg/dL)		Protein (mg/dL)		Total white blood cell count (cells/microL)		
	<10[¶]	10 to 40[Δ]	100 to 500[◇]	50 to 300[§]	>1000	100 to 1000	5 to 100
More common	Bacterial meningitis	Bacterial meningitis	Bacterial meningitis	Viral meningitis Nervous system Lyme disease (neuroborreliosis) Encephalitis Neurosyphilis TB meningitis[¥]	Bacterial meningitis	Bacterial or viral meningitis TB meningitis	Early bacterial meningitis Viral meningitis Neurosyphilis TB meningitis
Less common	TB meningitis Fungal meningitis	Neurosyphilis Some viral infections (such as mumps and LCMV)		Early bacterial meningitis	Some cases of mumps and LCMV	Encephalitis	Encephalitis

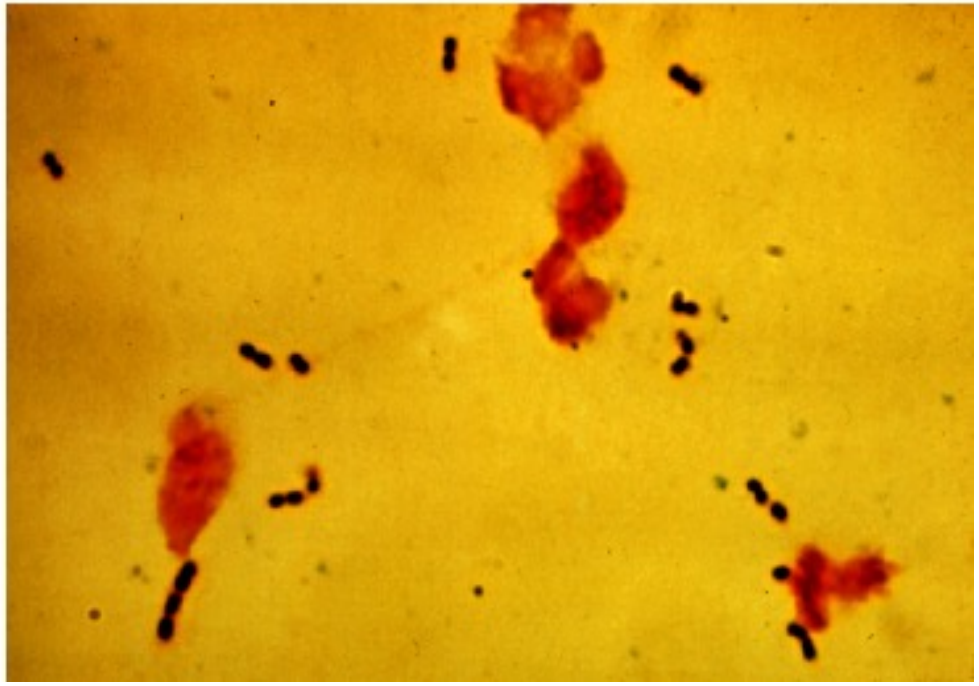
TB: tuberculosis; LCMV: lymphocytic choriomeningitis virus.

Source: UpToDate

How often is a CSF gram stain positive in bacterial meningitis?

- If done prior to antibiotics:
  - 90% for *Streptococcus pneumoniae*
  - *86% for Haemophilus influenzae*
  - *75% for Neisseria meningitidis*
  - *50% for* gram-negative bacilli
  - *33% for Listeria monocytogenes*

Yield may be ~ 20% lower in patients who received prior antibiotics



Meningitis/Encephalitis Multiplex PCR Panels

BACTERIA

- *Escherichia coli* K1
- *Haemophilus influenzae*
- *Listeria monocytogenes*
- *Neisseria meningitidis*
- *Streptococcus agalactiae*
- *Streptococcus pneumoniae*

VIRUSES

- Cytomegalovirus (CMV)
- Enterovirus (EV)
- Herpes simplex virus 1 (HSV-1)
- Herpes simplex virus 2 (HSV-2)
- Human herpesvirus 6 (HHV-6)
- Human parechovirus (HPeV)
- Varicella zoster virus (VZV)

YEAST

- *Cryptococcus (C. neoformans/C. gattii)*

Clinical Case

- A 54 year old man with type 2 diabetes mellitus presents to the ED with 48 hours of worsening headache, fever and neck stiffness. Exam is notable for otitis media on the left. Temperature 101.8 F, HR 104, RR 18, BP 130/80. Lumbar puncture is performed: glucose 20 mg/dL, protein 200 mg/dL, WBC 1,500. Gram stain shows gram positive diplococci.

- **What is your next step in management?**

A. Start ceftriaxone 2 gm IV q12 hours, vancomycin and ampicillin.

B. Start ceftriaxone 2 gm IV q12 hours plus vancomycin.

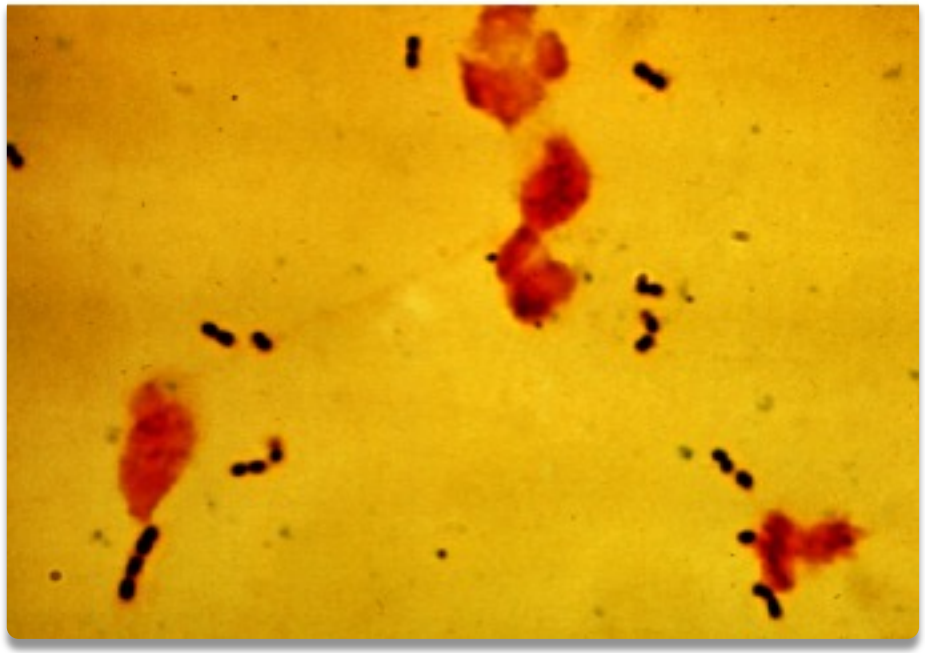
C. Start dexamethasone 0.15 mg/kg IV q6 hrs then start appropriate antibiotics 15-20 minutes later.

Role of Steroids in Meningitis

- In a 2002 prospective, randomized, placebo-controlled double-blind multicenter trial in adults patients were randomized to receive dexamethasone (10 mg q6h x 4 days) or placebo (first dose 15–20 min prior to the first antibiotics).
- At 8 weeks after enrollment, the percentage of patients with an unfavorable outcome (15% vs. 25%; p = .03) and death (7% vs. 15%; p = .04) was significantly lower in the dexamethasone group.

De Gans van de Beek D. Dexamethasone in adults with bacterial meningitis , *N Engl J Med*, 2002 , vol. 347 (pg. 1549-56)

Role of Steroids in Meningitis



- But, the benefit was entirely driven by the subgroup with Streptococcus pneumoniae infection
- Patients with S. pneumoniae meningitis in the dexamethasone group had a much lower percentage of unfavorable outcomes (26% vs. 52%; P = .006) and deaths (14% vs. 34%; P = .02)

IDSA Guidelines Recomendation

- "On the basis of the available evidence on the use of adjunctive dexamethasone in adults, we recommend use of dexamethasone (0.15 mg/kg q6h for 2–4 days with the first dose administered 10–20 min before, or at least concomitant with, the first dose of antimicrobial therapy) in adults with suspected or proven pneumococcal meningitis (A-I)"

Pneumococcal meningitis

- Most common cause of bacterial meningitis in US adults (~50% of cases)
- Can sometimes present with a concomitant otitis or sinusitis
- In the US where the incidence of ceftriaxone-intermediate or resistant pneumococcus is ≥1 percent empiric therapy includes vancomycin (15 to 20 mg/kg IV every 8 to 12 hrs)
  plus ceftriaxone (2 g IV every 12 hours)

Pneumococcal Vaccine Timing for Adults

Make sure your patients are up to date with pneumococcal vaccination.

Adults ≥50 years old
Complete pneumococcal vaccine schedules

Prior vaccines	Option A	Option B
None*	**PCV20 or PCV21**	**PCV15** → ≥1 year† → **PPSV23¶**
PPSV23 only at any age	≥1 year → **PCV20 or PCV21**	≥1 year → **PCV15**
PCV13 only at any age	≥1 year → **PCV20 or PCV21**	NO OPTION B
PCV13 at any age & **PPSV23** at <65 yrs	≥5 years → **PCV20 or PCV21**	

* Also applies to people who received PCV7 at any age and no other pneumococcal vaccines

¶ If PPSV23 is not available, PCV20 or PCV21 may be used

† Consider minimum interval (8 weeks) for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak (CSF) leak

§ For adults with an immunocompromising condition, cochlear implant, or CSF leak, the minimum interval for PPSV23 is ≥8 weeks since last PCV13 dose and ≥5 years since last PPSV dose; for others, the minimum interval for PPSV23 is ≥1 year since last PCV13 dose and ≥5 years since last PPSV23 dose

Clinical Guidance: Serotype 4

PCV21 contains eight new pneumococcal serotypes not included in PCV15, PCV20, or PPSV23. However, PCV21 doesn't contain certain pneumococcal serotypes (e.g., serotype 4) included in other pneumococcal vaccines.

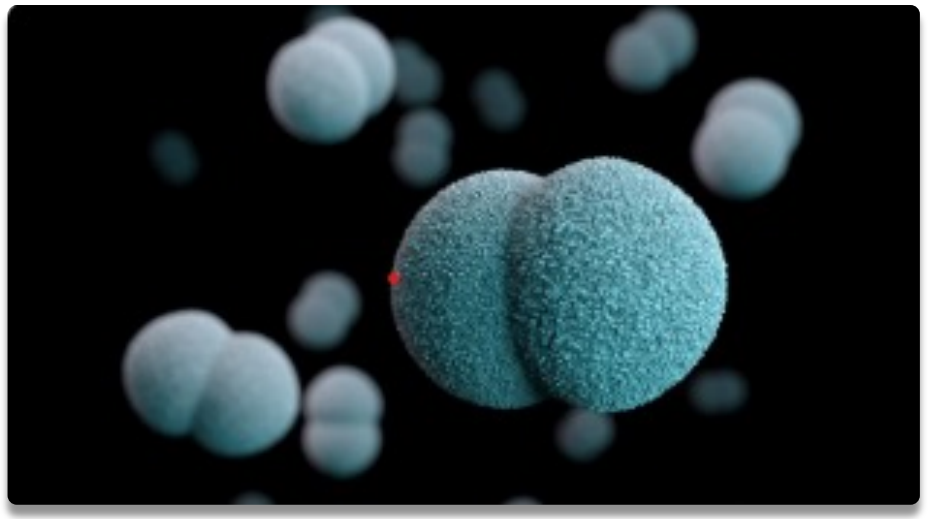
In certain adult populations in the Western United States with data (Alaska, Colorado, New Mexico, Navajo Nation, and Oregon), serotype 4 has caused high percentages (i.e., ≥30%) of invasive pneumococcal disease (IPD). We currently don't know if this is seen in other parts of the Western United States that don't routinely monitor IPD data.

Typically, individuals living within these geographic areas who develop serotype 4 IPD are adults aged <65 years with specific underlying conditions or risk factors such as alcoholism, chronic lung disease, cigarette smoking, homelessness, and injection drug use. Importantly, these individuals usually haven't received a PCV containing serotype 4. In such populations, other recommended pneumococcal vaccines (e.g., PCV20 alone or both PCV15 and PPSV23) are expected to provide broader serotype coverage against locally circulating strains compared to PCV21 alone.

Source: CDC PneumoRecs VaxAdvisor

Neisseria meningitidis

- N. meningitidis is a gram negative diplococcus spread by large respiratory droplets or direct contact with respiratory secretions
- Droplet plus standard precautions are recommended until 24 hour after initiation of appropriate antimicrobial therapy
- Second most common cause of bacterial meningitis in the US (~30-40% of cases)



Neisseria meningitidis meningitis

- Can have a very severe sometimes fulminant clinical presentation with vascular collapse due to release of lipooligosaccharide endotoxin
- May cause characteristic skin manifestations, such as petechiae and palpable purpura
- May also have associated septic arthritis

Post-exposure Prophylaxis (PEP)

- Chemoprophylaxis (usually with ciprofloxacin 500 mg x 1) is indicated for close contacts of patients with Meningococcal infection and should be given as early as possible following the exposure

- Although "close contact" has not been clearly defined, it generally refers to individuals who have had prolonged (>8 hours) contact while in close proximity (<3 feet) to the patient or who have been directly exposed to the patient's oral secretions during the 7 days before the onset of the patient's symptoms and until 24 hours after initiation of appropriate antibiotic therapy

Meningococcal Vaccines

MenACWY vaccination

11- to 12-year-old adolescents

Booster dose at age 16 years

Adults with functional asplenia, complement deficiency, HIV give at time of diagnosis and boost every 5 years

MenB Vaccination

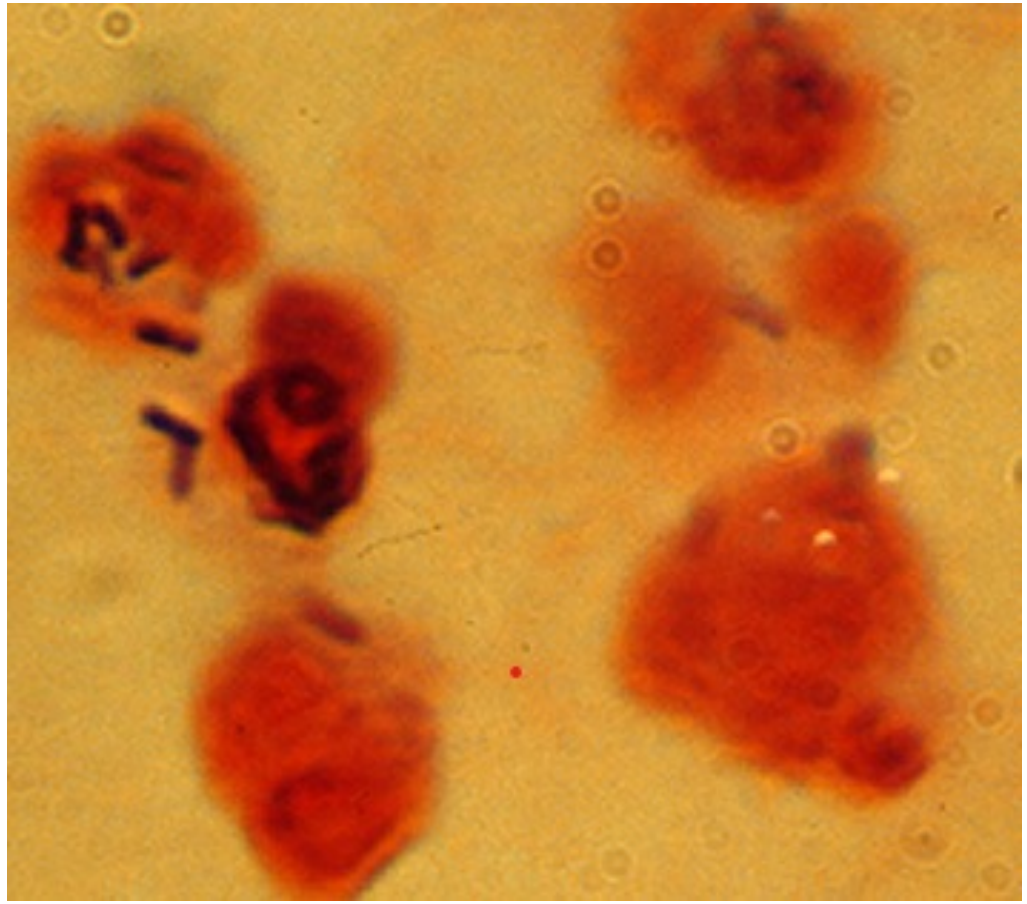
Shared decision making in patients age 16-23

Serogroup B meningococcal disease cases most commonly affect young adults who attend a four-year university, are freshmen, live in on-campus housing, or participate in sororities or fraternities

Listeria monocytogenes meningitis

- Short gram-positive rod that can occur singly or in short chains; can sometimes be confused with diphtheroids (Corynebacteria) or be gram variable and confused with Haemophilus

- More common in adults 50 and up and can sometimes cause a rhombencephalitis (encephalitis involving the brainstem and/or cerebellum) with cranial nerve abnormalities, ataxia, tremors, hemiplegia, deafness or seizures

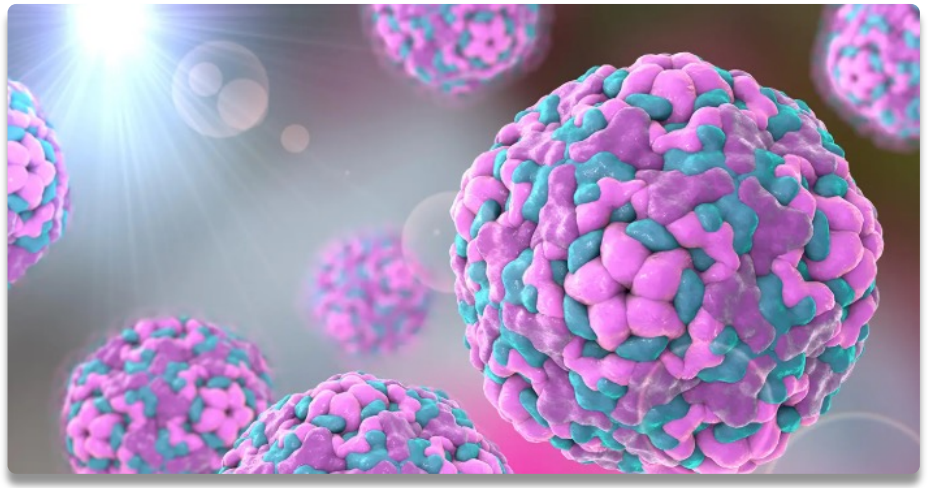


Listeria meningitis treatment considerations

- Ampicillin or penicillin with consideration of addition of an aminoglycoside is the IDSA recommended treatment
- Bactrim or meropenem are alternative agents for patients with penicillin allergies
- Optimal duration of treatment is unknown; some experts treat for 3-4 weeks (or longer in immunocompromised patients)

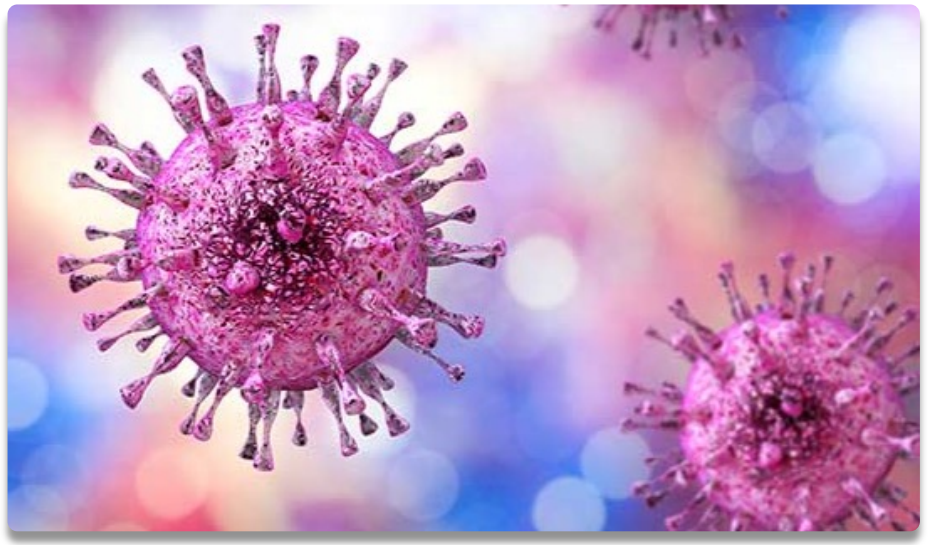
Enterovirus and Parechovirus Meningitis

- Ubiquitous picornaviruses found throughout the world that are transmitted from person to person through fecal-oral contact and, less commonly, respiratory secretions
- Patients may have pharyngitis and viral respiratory symptoms along with the meningitis
- 5-10% of patients may have diminished consciousness or seizures



HSV 2 Meningitis

- In contrast to HSV encephalitis, which is almost exclusively due to HSV-1, viral meningitis in immunocompetent adults is generally caused by HSV-2
- More commonly seen in young females with 50 percent having a history of genital herpes
- Most common cause of Mollaret meningitis (recurrent meningitis)



Meningitis Case

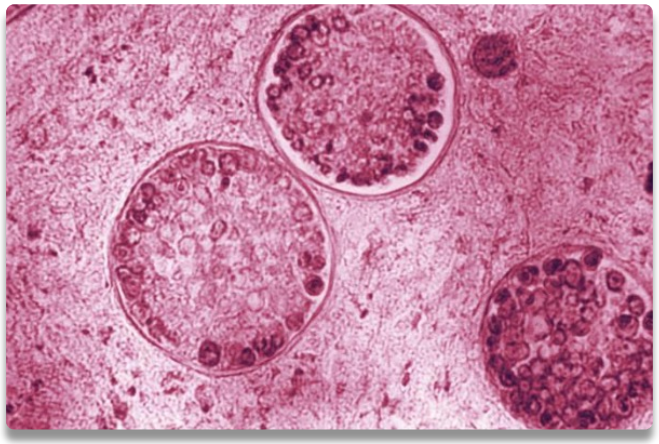
A 78 year old woman is brought to primary care clinic by her family with ~ 6 weeks of worsening daily headaches and back and neck pain. She lives locally during the summer but in winter she goes to live with a daughter in Phoenix. Her family has noticed that since she came back to the local area 2 months ago she has been forgetting things and seems confused. A CT head done by her PCP shows basilar leptomeningeal enhancement. She undergoes a lumbar puncture with glucose 10 mg/dL, protein 250 mg/dL, WBC 300 (80% lymphocytes, 10% eosinophils).

What is the most likely diagnosis?

A. Listeria meningitis
B. Coccidioides meningitis
C. TB meningitis
D. Neurosyphilis

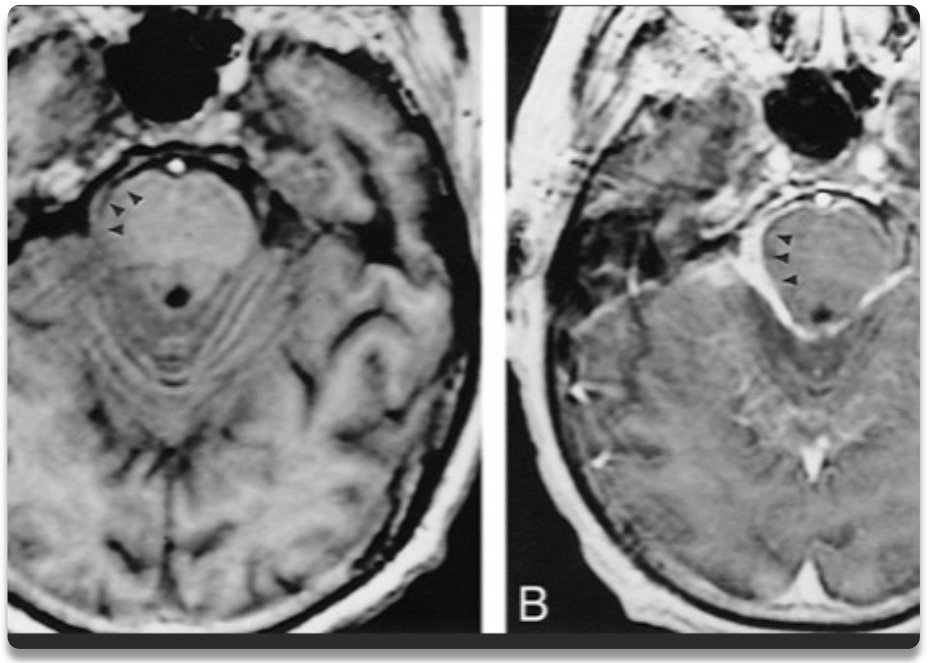
Coccidioides Meningitis

- Caused by the dimorphic fungi of the genus Coccidioides (C. immitis and C. posadasii), which are endemic in regions of the Southwestern United States
- If CNS disease develops it is usually within weeks to months after primary (pulmonary) infection
- May presents with worsening chronic headache, N/V, changes in mental status, back pain (if lumbar meninges involved)



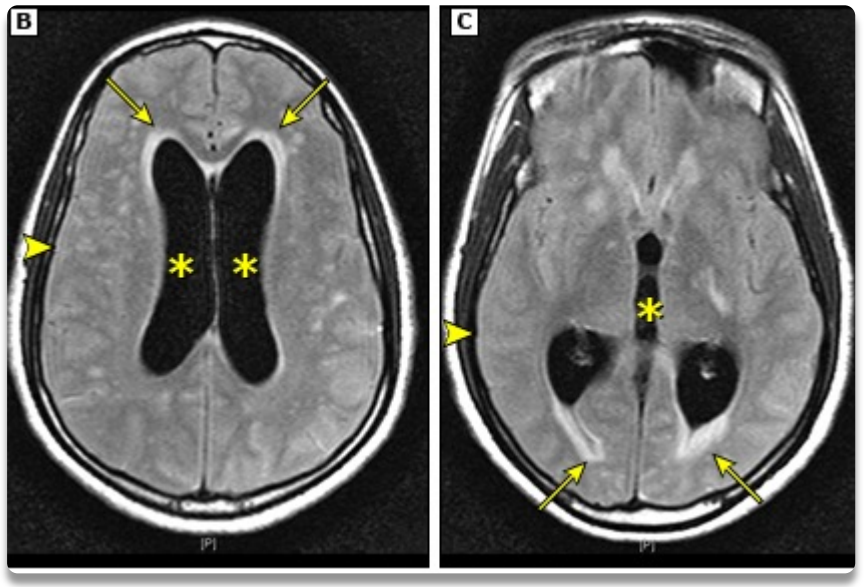
Coccidioides Meningitis: Diagnosis

- Basilar leptomeningeal enhancement is common on CT or MRI
- Hydrocephalus occurs in 30-50% of patients (may require shunt decompression)
- Coccidioides species will only grow from CSF culture ~ 15 % of the time so detection of complement-fixing (CF) IgG antibodies by immunodiffusion is often used for diagnosis



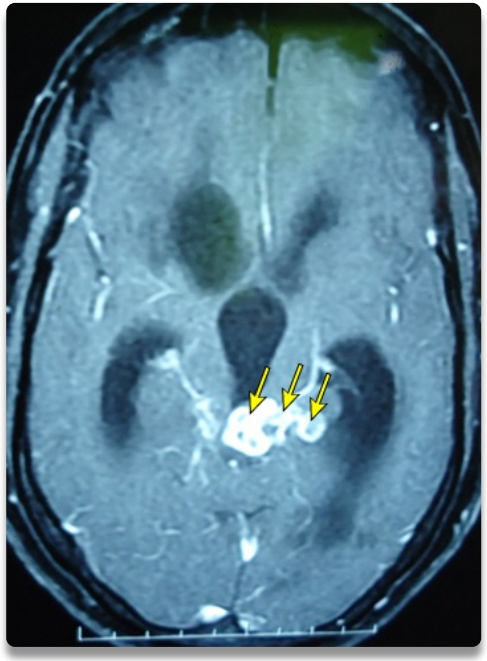
TB Meningitis

- 1-5% of TB cases are complicated by CNS involvement
- May have a subacute presentation (symptoms develop over weeks rather than days)
- Presence of cranial nerve palsies (most frequently involving cranial nerve III and VI) and hydrocephalus are common



TB Meningitis: Diagnosis

- Sensitivity of CSF AFB staining is 30-60%
- Diagnostic yield is increased with volume of CSF (up to 10-15 mL) and number of CSF specimens (up to 4)
- Sensitivity of CSF AFB culture for diagnosis of tuberculous meningitis is often < 50 %. CSF adenosine deaminase is often elevated.



Questions/Comments

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